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10/813,324	03/29/2004	Heidi A. Tissenbaum	UMY-035RCE	5837

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,324	TISSENBAUM ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,14,15,17-26,34-44 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,14,15,17-20,24-26,34-39,41-44 and 57* is/are rejected.

7)☒ Claim(s) *21-23 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Formal Matters

Claims 1, 14, 15, 17-20, 24-26 and 34-37 are amended. Claim 57 is new. Claims 3-13, 16, 27-33 and 45-56 are newly cancelled. Claims 1, 14, 15, 17-26, 34-44 and 57 are under examination.

Rejections/Objection Withdrawn

Any objection or rejections of claims 3-13, 16, 27-33 and 45-56 as set forth in the Office action mailed 27 October 2009 are withdrawn due to Applicants' cancellation of those claims.

Claim Rejections - 35 USC § 102

The rejection of claims 14, 15, 17-22, 24-26 and 34, 38-44 under 35 U.S.C. 102(b) as being anticipated by Ruvkun et al. (US Patent Application publication 2001/0029617, of record) as set forth in the Office action mailed 27 October 2009 is withdrawn in response to Applicants' amendment of the claims. In short, the prior art does not teach that the cholinergic pathway molecules are limited to EGL-8, RIC-8 and RIC-4, but rather it only teaches muscarinic receptors, which the claims no longer recite.

Claim Rejections - 35 USC § 103

The rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Ruvkun et al. (US Patent Application 2001/0029617; of record), and further in view of Gems & Riddle (Genetics, 2000; 154: 1597-1610) as set forth in the Office action mailed 27 October 2009 is withdrawn in response to Applicants' amendment of the claims. In short because Ruvkun et al. do not teach that the cholinergic pathway molecules are limited to EGL-8, RIC-8 and RIC-4, but rather it only teaches muscarinic receptors, which the claims no longer recite, Ruvkun et al. is no longer suitable as a primary reference.

The rejection of claim 23 under 35 U.S.C. 103(a) as being unpatentable over Ruvkun et al. (US Patent Application 2001/0029617; of record) as applied to claims 14, 15, 17-22, 24-26 and 34, 38-44 as set forth in the Office action mailed 27 October 2009 is withdrawn in response to Applicants' amendment of the claims. In short because Ruvkun et al. do not teach that the cholinergic pathway molecules are limited to EGL-8, RIC-8 and RIC-4, but rather it only teaches muscarinic receptors, which the claims no longer recite, Ruvkun et al. is no longer suitable as a primary reference.

The rejection of claims 20 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruvkun et al. (US Patent Application 2001/0029617; of record) as applied to claims 14, 15, 17-22, 24-26 and 34, 38-44 as set forth in the Office action mailed 27 October 2009 is withdrawn in response to Applicants' amendment of the claims. In short because Ruvkun et al. do not teach that the cholinergic pathway

molecules are limited to EGL-8, RIC-8 and RIC-4, but rather it only teaches muscarinic receptors, which the claims no longer recite, Ruvkun et al. is no longer suitable as a primary reference.

New Objection/Rejection

Claim Objections

Claims 21-23 and 40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14, 15, 17-20, 24-26, 34-39, 41-44 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for carrying out the claimed methods in a nematode having altered activity or expression of a cholinergic pathway molecule selected from the group consisting of EGL-8, RIC-8 and RIC-4 and altered activity in DAF-2; or alternatively carrying out the claimed methods in a nematode having altered activity or expression of a cholinergic pathway molecule selected from the group consisting of EGL-8, RIC-8 and RIC-4, does not reasonably

provide enablement for as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. ***This rejection was necessitated by Applicants' amendment.***

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(i) Regarding claims drawn to the insulin signaling pathway, which is now limited in the claims to DAF-2, Applicants submitted evidence in their response 7 May 2007 that they were enabled for all organisms, including mammals and humans, citing several articles as evidence, because the insulin receptor/IGF-I pathways were involved in longevity across all organisms. According to Applicants remarks submitted 11 August 2009, the mammalian analogue of DAF-2 is IGF-I and according to Barbieri et al. (of record; submitted by Applicants 7 May 2007) DAF-2 is 34% analogous with IGF-IR. Barbieri et al. teach that a study of centenarians showed increased sensitivity to insulin compared to younger subjects and low levels of IGF-I and that there are some

evolutionarily conserved mechanisms from worms to humans in insulin signaling and longevity (see E1068, right column). Barbieri et al. caution at p. E1069 (left column) that "whereas IGF-I signaling in long lived mutant and knockout mice is similar to the finding of reduced insulin/IGF-I signaling in long lived mutant invertebrates...in humans "insulin receptor mutations cause diabetes rather than longevity." Similarly, Klöting et al. (of record; submitted by Applicants 7 May 2007) teach that in humans, while "polymorphisms in the IGF-1 receptor gene and genotype combinations in IGF-IR and PI3KCB genes are associated with low levels of free plasma IGF-I, [and] are more frequent among long-lived people…severe, generalized loss of function mutations in insulin receptor function lead to severe insulin resistance and diabetes," thus ultimately shortening lifespan (see also Katic and Kahn, CMLS, 2005; 62: 320-343 at pages 333, right column, through 334, left column). The mutations of daf-2 described in the instant specification are loss of function mutations (for example see Examples 5-7 in the instant specification), and as noted above, such mutations do not result in longer life spans in humans.

(ii) The recitation of cholinergic pathway molecules in the claims with regard to both humans and mammals in general is not enabled. Regarding the involvement of the cholinergic pathway in human and mammalian aging, the art focuses on the declining density of muscarinic receptors in the aging brain. For instance, Fordyce et al. (of record) teach that exercise and caloric restriction can compensate for age-related decline in muscarinic receptor density. The claims, however, no longer recite muscarinic receptors and while the art teaches that the declining density of muscarinic

receptors in the aging brain, it is silent with respect to the mammalian homologues of EGL-8, RIC-4, or RIC-8 and a reduction in senescence in mammals. Undue experimentation would be required of the skilled artisan to determine a nexus between the mammalian homologues of EGL-8, RIC-4, or RIC-8, cholinergic signaling, and extension of the mature life phase of an organism. Thus with respect to the cholinergic pathway, the claims are not enabled for anything other than utilizing nematodes to screen for agents. Further, Applicants' evidence submitted 7 May 2007 in support of enablement for humans and mammals only focuses on the insulin/IGF-I signaling pathway and not upon the cholinergic pathway molecules as currently recited in the claims.

Due to the large quantity of experimentation necessary to carry out the claimed methods in species other than worms or mice, the lack of direction/guidance presented in the specification regarding and the absence of working examples directed to the same, the complex nature of the invention (identification of agents capable of extending the mature life phase of an organism), and the breadth of the claims which fail to recite limitations on the encompassed organisms, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

Claims 1, 14, 15, 17-20, 24-26, 34-39, 41-44 and 57 are rejected. Claims 21-23 and 40 contain allowable subject matter.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

/Bridget E Bunner/
Primary Examiner, Art Unit 1647